

SMALL CELL LUNG CANCER IN A YOUNG PATIENT WITH OSTEOPETROSIS

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Background: Osteopetrosis or Albers-Schönberg's disease is a heterogeneous group of rare hereditary troubles of the bone characterized by bone sclerosis due to an alteration of the bone reabsorption mediated by osteoclasts. The defect in the osteoclastic activity is responsible for complete or partial medullary cavities occlusion, with consequent reduced hemopoiesis, and for the excessive fragility of the affected bone segments.

Case report: We reported the case of a young man of 31 years affected by osteopetrosis in which a small cell lung cancer developed.

Key words: lung cancer, osteopetrosis, young.

Results: Small cell lung cancer is a particularly rare neoplasm in the young, and even though it is highly sensitive to chemotherapeutic treatment its prognosis remains poor. The greatest clinical problem connected with chemotherapeutic treatment of patients affected by osteopetrosis is the variability of the reduction of their bone marrow reserve, which could expose them to an excessive hematological toxicity caused by the therapy.

Conclusions: The adoption of suitable prophylactic measures, such as the use of growth factors and drugs selected in relation to their toxicity or given in reduced doses, should be appropriately considered in these subjects.

Introduction

Osteopetrosis (OP) or Albers-Schönberg's disease is a heterogeneous group of rare hereditary troubles of the bone characterized by bone sclerosis due to an alteration of bone reabsorption mediated by osteoclasts¹. The defect in the osteoclastic activity, which has been related to mutation of the gene of M-CF in an animal model², is responsible for complete or partial medullary cavities occlusion, with consequent reduced hemopoiesis, and for the excessive fragility of the affected bone segments.

OP is divided into one infantile malignant form and an intermediate form, both autosomal recessive, and a benign autosomal dominant form of the adult. The dominant form, relatively benign³, can be diagnosed with radiological examinations in adults without any symptoms, or alternatively the affected subject can complain of diffuse bone pain, fractures, osteomyelitis, dentition alterations, cephalaea, vision and auditory defects due to compression of the cranial nerves. Typical hematological troubles of the infantile and intermediate forms of OP, such as anemia, thrombocytopenia and leukopenia, were described in the dominant form as well⁴.

Cases in which subjects affected by Albers-Schönberg's disease develop a neoplasia are rare⁵⁻¹⁰ and, according to literature data, the association of the disease with solid tumors has been described in two patients so far^{9,10}. The case that came under our observation, a young man 31 years of age affected by osteopetrosis in which a small cell lung cancer developed, shows the unusual association of the two diseases.

Small cell lung cancer is indeed a particularly rare neoplasm in the young¹¹ and even though it is highly sensitive to chemotherapeutic treatment, its prognosis remains poor. Together with the clinic case description, considering the rarity of the event, we discuss the clinic features connected with the diagnosis of lung cancer in the young and with the chemotherapeutic management of the neoplasm complicated by the contemporaneous presence of Albers-Schönberg's disease as well.

Case report

In July 2002, a 31-year-old white male came under our observation for persistence of an intense bilateral lumbar-sciatic pain for about three months. History revealed the sudden onset of the symptoms consequent to a violent physical effort made by the patient and the little benefit obtained from the irregular consumption of NSAIDs in those months. Moreover, substantial consumption of tobacco (40 cigarettes a day since the age of 18) as well as alcoholic drinks by the young man emerged. X-ray of the skeleton (Figure 1) showed bone sclerosis in all the examined segments, which is a characteristic radiological sign of OP. An analgesic therapy with NSAIDs (diclofenac, 50 mg twice a day) was prescribed. After about 20 days, the man presented again, showing a general decline in his state of health and complaining of the appearance of dyspepsia, slight fever, fatigue, cough, anorexia and a marked weight loss. Clinical examination revealed abdominal pain upon palpation of the epigastric region, reduction of the

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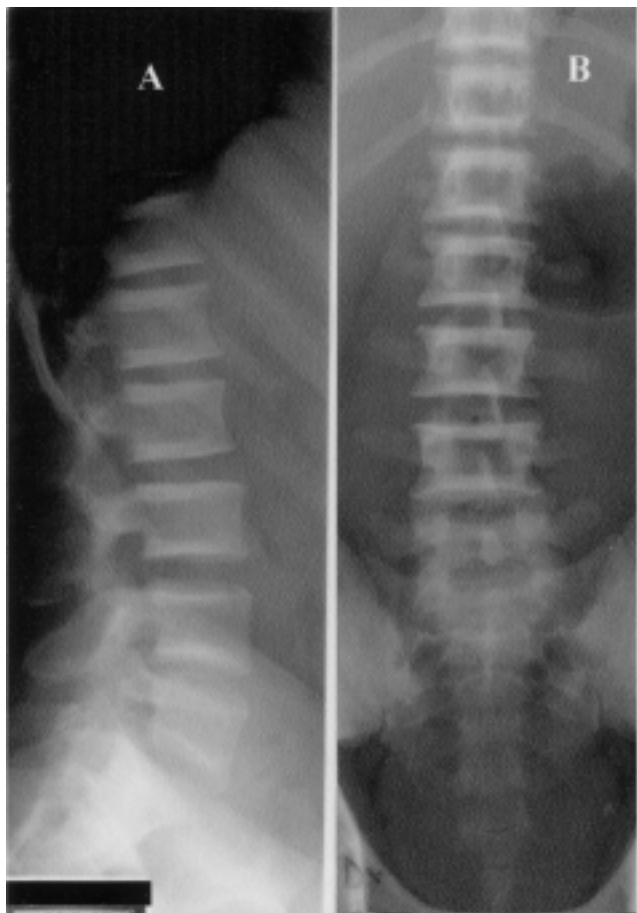


Figure 1A and B - X-ray of the vertebral column shows bone sclerosis, which is a characteristic radiological sign of OP.

vesicular murmur at the base of the left lung, and the presence of partial tooth loss and decay in his mouth.

Laboratory findings showed slight anemia (HGB, 11.0 g/dl), hepatic sufferance (AST, 73 IU/L; ALT, 67 IU/L; LDH, 4714; alkaline phosphatase, 144 IU/l) and high serum levels of CK-MB (519 IU/l).

CT scan of the thorax and abdomen (September 9th) showed (Figure 2) the presence of an expansive mass in the lower lobe of the left lung and several swollen mediastinic lymph nodes, It also highlighted many metastatic liver lesions.

A bronchoscopy with lung biopsy was performed, and the histological examination diagnosed a small cell lung cancer (September 24th) (Figure 3). The neoplasm was at the IV stage. The patient was treated with palliative chemotherapy, and the CAV schedule was administered (cyclophosphamide, 1000 mg/m² day 1; doxorubicin, 40 mg/m² day 1; vincristine, 1 mg/m² day 1, every 21 days) with dose reduction to 75% because of his presumed reduced bone marrow reserve.

Only one treatment cycle was administered. It did not lead to an important hematological toxicity, except for neutropenia (Neu 700 × mm³), which did not require



Figure 2 - Thorax CT scan shows the neoplastic mass in the base of the left lung.

specific treatment. CT brain scan (October 4th), requested to complete staging, showed a metastatic lesion of about 3 mm of diameter in the frontal left lobe; it also revealed a condition of hydrocephalus.

Palliative radiotherapy on the brain was not performed. In fact, since the 2nd week of October the patient fell into a more and more serious decline of his state of health. In those days, several skin metastases suddenly appeared in every part of his body (Figure 4). Progressive complications of his respiratory function together with the onset of neoplastic cachexia led to his death on November 2nd.

Discussion

Only a few cases have been reported in which patients affected by Albers-Schönberg's diseases develop a malignancy⁵⁻¹⁰ in the course of their life. The most frequently described association is that between OP and hematological neoplasms such as lymphomas^{5,6} and leukemias^{7,8}. Till now, the association between OP and solid tumors has been described only in relation to a case of esophageal carcinoma or to a case of lung carcinoma¹⁰. The latter, diagnosed only after the patient's death, was given no treatment.

Anyhow, it is difficult to estimate the chances of developing a neoplasm in a patient affected by OP during his life. This is probably due to the low incidence of OP, added to the fact that infantile forms usually lead to a premature death^{12,13} and that adult forms often remain undiagnosed because they do not show important symptoms.

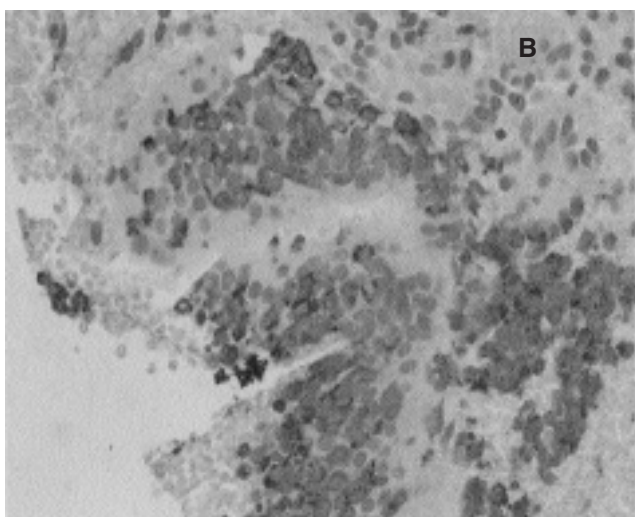
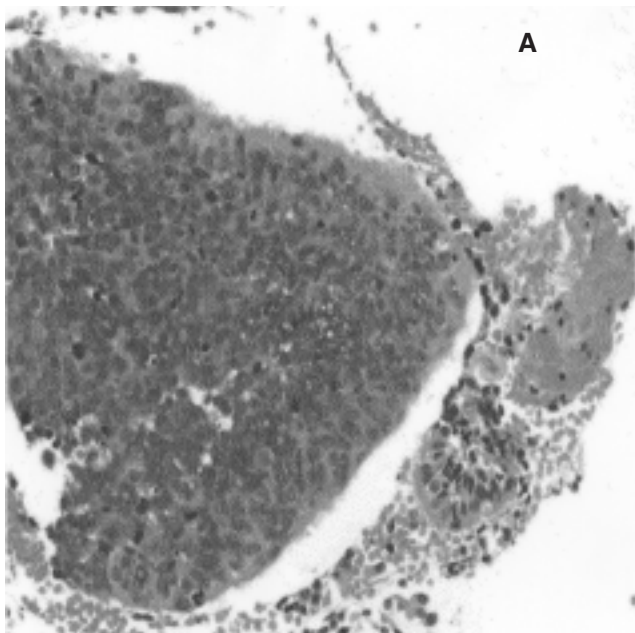


Figure 3A and B - A biopsy of the pulmonary mass diagnosed a small cell lung cancer. Immunohistochemistry showed positivity of neoplastic cells for chromogranin.

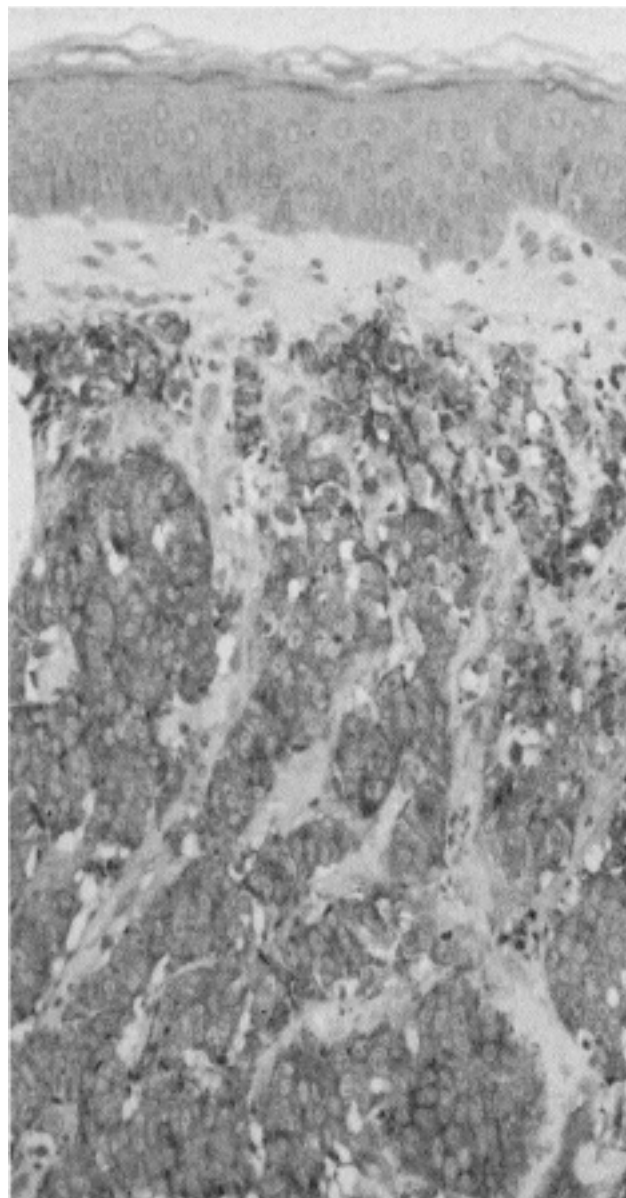


Figure 4 - Biopsy of the skin: the figure shows a cutaneous metastasis by small cell lung cancer. The neoplastic cells are positive for synaptophysine. This aspect confirms neuroendocrine nature of these cells.

In the reported case, a 31-year-old young male who was discovered by chance to be affected by Albers-Schönberg's disease in its dominant form, developed a small cell lung cancer. The OP dominant form and small cell lung cancer are both rare diseases in young men. The accidental discovery of the presence of the adult dominant variant of Albers-Schönberg's disease happens in about 50% of the cases¹⁴ because of the symptoms scarcity. Small cell lung cancer is a frequent neoplasia in the general population but it is uncommon in subjects under the age of 40¹¹. As in our case, the diagnosis of lung cancer in the young man is often made

late because the symptoms are usually undervalued and minimized until the disease arrives to an advanced stage, due to the rarity of the condition¹⁰.

In this occasion despite the need to begin a chemotherapeutic treatment quickly, in order to face advanced and extremely aggressive neoplasm, we had to consider the particular comorbidity the young man presented. The greatest clinical problem connected with chemotherapeutic treatment of patients affected by OP is indeed the variability of the reduction of their bone marrow reserve which could expose them to an excessive hematological toxicity caused by the thera-

py. In fact, even though hematological troubles such as anemia, thrombocytopenia and leukopenia are more typical of the infantile or intermediate forms, it is possible to find them in the adult variant of OP as well⁴. That is why we decided to treat the patient with effective drug doses reduced to 75%, and after the only treatment cycle carried out we noticed the appearance of grade 3 neutropenia which did not require specific treatment. The considerable decline of the general state of health shown by the young man later caused

chemotherapy interruption, therefore it was not possible to weigh its impact on the bone marrow function. Anyhow, it is reasonable to suppose that OP may be an important comorbidity cause in patients affected by a neoplasm who have to undergo chemotherapeutic treatment, and the adoption of suitable prophylactic measures such as the use of growth factors, drugs selected in relation to their toxicity or given in reduced doses, should be appropriately considered in these subjects.

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